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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,346	05/15/2001	Natarajan Ranganathan	KBI-0004	9305

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EXAMINER
DAVIS, RUTH A

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/19/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,346	RANGANATHAN ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *11-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's amendment has been received and entered into the case. Claims 1 – 16 are pending.

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1 - 10 in Paper No. 5 and traversal arguments in paper No.7, is acknowledged. The traversal is on the ground(s) that all claims are drawn to the same subject matter, that a search for one group would be the same as the other, and that there is no burden on examiner. This is not found persuasive because as stated in the previous office action, while the search for each of the inventions may overlap, an overlapping search is not a coextensive search. Furthermore, as evidenced by the separate classification, the inventions are distinct and separate. A reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

The requirement is still deemed proper and is therefore made FINAL.

Therefore, claims 1 – 16 are pending, claims 11 – 16 have been withdrawn from consideration and claims 1 – 10 have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1 – 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and its dependents are drawn to a pharmaceutical composition, however are rendered vague and indefinite because it is unclear if the pharmaceutical prevents infection of a patient, or if the microencapsulation/enteric coating prevents infection.

In claim 1, line 8, "the sorbents" lacks sufficient antecedent basis.

Claim 10 is drawn to a pharmaceutical composition, however is rendered vague and indefinite because it is unclear if the pharmaceutical prevents infection of a patient, or if the microencapsulation/enteric coating prevents infection.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1 – 3 and 6 – 9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Paul ('099) in view of Ford).

Applicant argues that the references do no teach or suggest the new limitations of claim 1, that there is no expectation of success to combine the references. Applicant additionally argues that the composition of Paul is intended to bind to antigens, bacteria, fungi, viruses wherein the instant composition is without binding, that Ford teaches encapsulated bacteria for vaginal infections, and that the references do not teach or suggest preventing infection of the patient. Applicant additionally argues the references individually, in that Paul does not teach enteric coatings and Ford does not teach probiotics, prebiotics that are microencapsulated.

However, these arguments fail to persuade for the following reasons.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Ford specifically teaches that oral pharmaceutical compositions containing bacteria have a great advantage in therapeutic utility when they are microencapsulated (col.2 line 40-44). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Ford to microencapsulate the composition of Paul for the disclosed "great advantages" in that therapeutic utility is increased. Furthermore, while applicant argues the composition of Ford is intended to release the bacteria, it is pointed out that Ford uses sodium alginate (encapsulation method A, col.4) and hydroxycellulose (method C, col.5) as the coating materials, which are taught by applicant as suitable coatings for the instant composition (specification p.15). As such, it would appear that the coatings of Ford would achieve the desired effect as claimed and argued by applicant (specifically being substantially native in form, without binding digestive materials and preventing infection of the patient).

Regarding the binding of the composition of Paul, the claims are drawn to a composition which does not bind to digestive materials only. The claim language does not limit the claim to be without binding, but without binding digestive materials. Therefore, the fact that the composition of Paul does not bind to digestive materials would meet the limitation.

Regarding applicant's argument that Ford teaches encapsulated bacteria for vaginal infections, Ford specifically teaches oral pharmaceutical compositions comprising encapsulated bacteria (col.1 line 62-66, col.2 line 39-51, col.5 - 7) wherein the therapeutic utility has great advantages (col.2 line 40-44).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

For these reasons and those made previously of record, the claims stand rejected.

7. Claims 1 – 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paul ('988), Niisato, Hider, Yatzidis, and Giovannetti (Nephron, 1995) in view of Chang et al. (WO 97/26903).

Applicant claims a pharmaceutical composition comprising a probiotic, prebiotic and an ammonia-philic urea-degrading microorganism with high alkaline stability and urease activity, that is micro-encapsulated or enteric coated. The composition further comprises a water adsorbent selected from locust bean gum, psyllium fiber, guar gum and zeolite, and an adsorbent for inorganic phosphate and an adsorbent for uremic solutes other than urea wherein the adsorbent for phosphate is selected from aluminum hydroxide gel, calcium hydroxide gel and magnesium hydroxide gel and the uremic solute adsorbent is activated charcoal. The probiotic is a Bifidium or Lactobacillus, the prebiotic is a fructan oligosaccharide or and araban oligosaccharide, the ammonia-philic bacteria is selected from Bacillus pasteurii, Sporosarcina ureae, Bacillus species and Lactobacillus species KB-I. Alternatively the probiotic and ammonia-philic urea-degrading microorganism is the same species. Applicant additionally claims a pharmaceutical composition comprising a probiotic, prebiotic, an ammonia-philic urea-degrading microorganism with high alkaline stability and urease activity, a water adsorbent, an

adsorbent for inorganic phosphate and an adsorbent for uremic solutes other than urea, that is micro-encapsulated or enteric coated.

Paul teaches a composition for promoting gastrointestinal health comprising an effective amount of Lactobacillus and Bifidobacterium (Bifidum) (abstract). Specifically, Paul teaches Lactobacillus and Bifidobacteria inhibit toxic activities of bacteria in patients with chronic kidney failure (or uremia) (col.2 line 35-40).

Niisato teaches a composition containing fructooligosaccharides for preventing uremia and renal insufficiency (abstract).

Yatzidis teaches locust bean gum is an efficient sorbent upon uremic substances to include urea, chloride, uric acid, creatine, ammonia, phosphorus, and sodium (p.105).

Hider teaches that patients with kidney disorders/diseases who suffer from elevated phosphate levels are traditionally treated with phosphate adsorbents magnesium hydroxide, aluminum hydroxide, calcium hydroxide or mixtures thereof (col.1 line 6-17).

Giovannetti teaches oral administration of activated charcoal is effective for treating uremia (abstract).

The above references do not teach each of the ingredients together in a single composition. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to combine the instant ingredients for their known benefit, as disclosed by the cited references above, since each is well known in the art for treating and/or preventing uremia and kidney disease. Moreover at the time of the claimed invention, one of ordinary skill in the art would have been motivated by the above references to combine the instant ingredients

together with a reasonable expectation for successfully obtaining a composition effective to treat uremia and/or kidney diseases.

The references do not teach compositions that are micro-encapsulated or enteric coated. However, Chang teaches oral pharmaceutical compositions for treating kidney failure (p.4 line 24-28) wherein microorganisms are microencapsulated (abstract, p.11 line 24-28). Specifically, Chang teaches compositions where bacteria are encapsulated to prevent infection of the patient (p.1 line 19-25) and the compositions are used to remove urea and ammonia in treating kidney failure and uremia (p.1 line 29-33). Bacteria include Bacillus pastteuri (p.6 line 27-34) and coatings include polylactic acid, polyglycolic acid, chitosan alginate and hydroxy celluloses (p.4 line 5-12).

At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Chang to microencapsulate the composition obtained by the combined teachings above with a reasonable expectation of preventing patient infection and effectively treating kidney failure, diseases and uremia. Although Chang does not teach the coating maintains the bacteria in substantially native in form without binding digestive materials, the coatings used are the same as those disclosed by applicant (specification, p.15). As such, the coatings of Chang would have inherently accomplished the claimed effects. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by the cited references to combine the claimed ingredients together in encapsulated form with a reasonable expectation for successfully obtaining an effective composition for treating kidney diseases and/or uremia.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
November 15, 2002

LEON B. LANKFORD, JR.
PRIMARY EXAMINER